Pollen metabolome analysis reveals adenosine as a major regulator of dendritic cell-primed T(H) cell responses.

Abstract: Water-soluble components from pollen modulate dendritic cell (DC) functions, such as IL-12 secretion and 3'-5'-cyclic adenosine monophosphate (cAMP) signaling and migration, possibly contributing to the establishment of a T(H)2-dominated immune response against pollen. Because these effects could not solely be attributed to the previously identified pollen-associated lipid mediators, the pollen metabolome was analyzed for candidate immunomodulatory substances. We sought to perform an analysis of the effect of pollen-associated adenosine on DC function and T(H) cell differentiation. Fractions of aqueous pollen extracts (APEs) were generated by means of ultrafiltration and were subjected simultaneously to biological tests and metabolome analysis (ultra-high-resolution mass spectrometry) and ultraperformance liquid chromatography. Effects of pollen-derived adenosine on monocyte-derived DC cAMP signaling, cytokine response, and capacity to differentiate T(H) cells were studied. The less than 3-kd fraction of APEs comprised thousands of substances, including adenosine in micromolar concentrations. Pollen-derived adenosine mediated A2 receptor-dependent induction of cAMP and inhibition of IL-12p70 in DCs. APEs digested with adenosine deaminase failed to mediate IL-12
inhibition. DCs of nonatopic donors exposed to APEs showed an adenosine-dependent reduced capacity to differentiate T(H)1 cells and an enhanced capacity to induce regulatory T cells and IL-10. DCs of atopic donors failed to induce IL-10 but instead induced IL-5 and IL-13. This study identifies adenosine out of thousands of metabolites as a potent immunoregulatory substance in pollen. It acts on the level of the DC, with differential effects in atopic and nonatopic donors.